

What Is Claimed Is:

1. A nucleic acid construct for expressing an active substance which is activated by an enzyme which is released from mammalian cells, wherein said construct comprises the following nucleic acid sequences in the following order:

a) at least one promoter element operably linked to;

b) at least one nucleic acid sequence which encodes an active compound, wherein said active compound is endogenous to mammals, operably linked to;

c) at least one nucleic acid sequence which encodes an amino acid sequence cleavable specifically by an enzyme which is released from a mammalian cell, operably linked to;

d) at least one DNA sequence which encodes a polypeptide which is bound to said active compound by said cleavable amino acid sequence and inhibits the activity of said active compound, and wherein said nucleic acid component c) (does not naturally occur as operably linking said nucleic acid sequence b) to said nucleic acid d).

2. A nucleic acid construct as claimed in claim 1, wherein said enzyme is a protease.

3. A nucleic acid construct as claimed in claim 1, wherein said enzyme is a prostate specific antigen, a plasminogen activator, a cathepsin or a matrix metalloproteinase.

4. A nucleic acid construct as claimed in claim 1, wherein said mammalian cells are tumor cells, leukemia cells, endothelial cells, macrophages, lymphocytes,

Sub
AA2

[Handwritten scribbles]

21. A method for preparing a polypeptide which is encoded by said nucleic acid construct of claim 1, comprising transducing a suitable cell with said construct, expressing said polypeptide in said cell, and isolating said expressed polypeptide.

22. The method of claim 20, wherein said cell is an endothelial cell, a lymphocyte, a macrophage, a glia cell, a fibroblast, a liver cell, a kidney cell, a muscle cell, a cell of the bone or cartilage tissue, a synovial cell, a peritoneal cell, a skin cell, an epithelial cell, a leukemia cell or a tumor cell.

²/₂₃. The method of claim ²/₂₁, wherein said cell is an endothelial cell, a lymphocyte, a macrophage, a glia cell, a fibroblast, a liver cell, a kidney cell, a muscle cell, a cell of the bone or cartilage tissue, a synovial cell, a peritoneal cell, a skin cell, an epithelial cell, a leukemia cell or a tumor cell.

24. A cell transduced with said nucleic acid construct of claim 1.

25. A protein encoded by said nucleic acid construct of claim 1.

Sub D'
~~AA2~~

add
C2
Add
D2

muscle cells, epithelial cells, glia cells, synovial cells or virus-infected cells.

5. A nucleic acid construct as claimed in claim 1, wherein said nucleic acid construct further comprises a nucleic acid sequence operably linked to said construct of claim 1, wherein said nucleic acid sequence encodes a ligand which binds said active compound to a target structure.

6. A nucleic acid construct as claimed in claim 1, wherein said nucleic acid sequences b) and d) of claim 1 encode parts of a natural precursor of a protein active compound, wherein the nucleic acid sequence encoding the cleavage sequence naturally occurring between said nucleic acid sequences b) and d) has been replaced by said nucleic acid sequence c), which does not naturally occur between said nucleic acid sequences b) and d).

7. A nucleic acid construct as claimed in claim 1, wherein said polypeptide encoded by said nucleic acid sequence d) is part of a natural precursor of a protein active compound.

8. A nucleic acid construct as claimed in claim 1, wherein said construct is operably inserted into a plasmid or a viral vector.

9. A nucleic acid construct as claimed in claim 1, wherein said nucleic acid sequence a) is a promoter sequence which can be activated nonspecifically, cell-specifically, virus-specifically, metabolically, cell cycle-specifically or by tetracycline.

10. A nucleic acid construct as claimed in claim 1, wherein said nucleic acid sequence a) comprises at least two identical or two different promoter sequences.

11. A nucleic acid construct as claimed claim 9, wherein said nucleic acid sequence a) is activated in endothelial cells, in cells adjoining activated endothelial cells, in muscle cells, in leukemia cells, in tumor cells, in glia cells, in lymphocytes, in macrophages or in synovial cells.

12. A nucleic acid construct as claimed in claim 1, wherein said active compound activates or inhibits a biological activation cascade or is an active component of this cascade, or activates or inhibits the coagulation system, activates fibrinolysis, activates the complement system or activates the kinin system, or is an enzyme which converts the inactive precursor of a pharmacological substance into the active substance, or which itself is a pharmacologically active substance.

13. A nucleic acid construct as claimed in claim 12, wherein said active compound is a coagulation factor which is selected from the group consisting of thrombin, factor Va, factor VIIa, factor IXa, factor Xa, TF coagulation-active fragments or factor XIIa; thrombin which is mutated in the region of the Arg-Thr cleavage site (amino acid position 327/328); a fibrinolytic protein which is selected from urokinase, tPA or functional hybrids thereof; a complement factor which is selected from C3b, C5b or functional cleavage products thereof; an antithrombotic protein which is selected from protein C, C1s inhibitor, α 1-antitrypsin, hirudin, AT-III, TFPI, PAI-1, PAI-2 or PAI-3; a kallikrein; a cytostatic, cytotoxic or inflammation-eliciting protein; an antiangiogenic protein; an immunomodulatory protein;

an antiinflammatory protein; a protein which relieves damage to the nervous system; a protein which inhibits or neutralizes the neurotoxic effect of $\text{TNF}\alpha$; an angiogenesis-stimulating protein; a hypotensive protein; an antiviral protein; a cytokine; an interferon; a tumor necrosis factor; oncostatin M or LIF; a cytokine receptor; the moiety of a cytokine receptor which is external to the cell; a cytokine antagonist; a growth factor; a growth factor receptor; the moiety of a growth factor receptor which is external to the cell; a chemokine; angiostatin; platelet factor 4; TIMP-1, TIMP-2 or TIMP-3; a nitroreductase; a β -glucuronidase; a carboxypeptidase; a β -lactamase; a cytosine deaminase; a catalase; a peroxidase; a phosphatase; an oxidase; kallikrein or an endothelial cell nitric oxide synthase.

14. A nucleic acid construct as claimed in claim 1, which further comprises a nucleic acid sequence b') which encodes a ligand which binds to a cell membrane receptor, a cell membrane antigen, a cell membrane-located adhesion molecule, or to the extracellular matrix or component thereof.

15. A nucleic acid construct as claimed in claim 14, wherein said ligand is an antibody or an antibody fragment which binds specifically to a cell membrane antigen or to an antigen on the extracellular matrix, or is a polypeptide which binds to receptor on the cell membrane wherein said polypeptide is a growth factor, a cytokine, an interferon, a tumor necrosis factor, a chemokine, a receptor-binding part sequence of these ligands, a peptide hormone, angiotensin, kinin, folic acid, an adhesion molecule or the part sequence of the adhesion molecule which binds to the corresponding adhesion molecule or to the extracellular matrix, an extracellular moiety of an Fc receptor, a glycoprotein of

a virus, a part sequence of the glycoprotein which binds to these cells, the transmembrane domain of a receptor or of a viral glycoprotein, or a glycopospholipid anchor.

16. A nucleic acid construct as claimed in claim 14, wherein said ligand binds to activated or proliferating endothelial cells, to tumor cells, to muscle cells, preferably smooth muscle cells, to fibroblasts, to macrophages, to lymphocytes, to liver cells, to kidney cells, to synovial cells, to inflammatory cells, to virus-infected cells, to bronchial epithelial cells, to glia cells or to leukemia cells.

17. A nucleic acid construct as claimed in claim 14, wherein the construct comprises at least two identical or different nucleic acid sequences b)c)d) or b')b)c)d), which nucleic acid sequences are linked to each other by way of an internal ribosomal entry site.

18. A process for preparing a nucleic acid construct according to claim 1, which comprises operably linking said nucleic acid sequences of claim 1.

19. A method for the treatment or prophylaxis of tumors, leukemias, allergies, autoimmune diseases, infections, inflammations, transplant rejection reactions, thromboses, blood vessel occlusions, blood coagulation, blood circulation disturbances, injuries to tissues, or damage to the nervous system, comprising administering to a mammal an effective amount of a polypeptide expressed by the nucleic acid construct of claim 1.

20. A method for preparing a recombinantly altered cell, comprising transducing a suitable cell with said nucleic acid construct of claim 1.